Examiner: Binta M. Robinson

Date of Office Action: 19 JAN 2010 Applicant(s): Widmer et al. Date of Response: April 19, 2010

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the above identified application.

Listing of Claims:

 (Currently Amended):
 A eempound of bis-cationic compound wherein the biscation of the compound is of Formula (I)

$$\begin{matrix}R_1 \oplus \\ R_2 \longrightarrow Y_1 - C(R_7R_7) - (A) - C(R_8R_8) - Y_2 \swarrow R_5 \\ R_6\end{matrix}$$
(I)

wherein:

(1) Y₁ and Y₂ may be the same or different and are independently selected from N and P:

 R_1 to R_6 may be the same or different and are independently selected from the group consisting of optionally substituted $C_{1.10}$ alkyl, optionally substituted $C_{2.10}$ alkenyl, optionally substituted $C_{2.10}$ alkenyl, optionally substituted $C_{3.10}$ cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from $C_{1.6}$ alkyl, $C_{2.6}$ alkenyl, $C_{2.6}$ alkynyl, hydroxyl, halogen, $O(C_{1.6}$ alkyl), $O(O)O(C_{1.6}$ alkyl), $OC(O)(C_{1.6}$ alkyl), $OC(O)(C_{1$

Serial No.: 10/579,263 Examiner: Binta M. Robinson

Date of Office Action: 19 JAN 2010 Applicant(s): Widmer et al. Date of Response: April 19, 2010

 R_7 , R_7 , R_8 and R_8 may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted $C_{5.7}$ cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from $C_{1.6}$ alkyl, $C_{2.6}$ alkenyl, $C_{2.6}$ alkynyl, hydroxyl, halogen, NO_2 , $C(O)R_{10}$, OR_{11} , CH_2OR_{11} , $CH_2NR_{12}R_{13}$, SR_{11} , $NR_{12}R_{13}$, $CONR_{12}R_{13}$, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyn, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen;

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkynly, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substitutents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or

 R_{12} and R_{13} , together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from $C_{1.4}$ alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$;

and when $Y_1=Y_2=N$, A comprises one or more groups selected from substituted alkylene, substituted alkenylene, substituted phenyl, substituted C_{5-7} cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C_4 - C_6 alkyl, C_{4-6} alkenyl, C_{4-6} alkynyl, hydroxyl, halogen, NO_2 , $C(O)R_{10}$, OR_{11} , CH_2OR_{11} , $CH_2NR_{12}R_{13}$, SR_{11} , $NR_{12}R_{13}$, $CONR_{12}R_{13}$, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

Examiner: Binta M. Robinson
Date of Office Action: 19 JAN 2010
Applicant(s): Widmer et al.
Date of Response: April 19, 2010

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyn, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen;

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or

R₁₂ and R₁₃, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C₁₋₄ alkyl, hydroxyl, halogen, amino, and C(O)OR₁₁:

and when $Y_1 = Y_2 = P$, A comprises one or more groups selected from substituted alkylene, substituted alkenylene, substituted phenyl, substituted C_{5-7} cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, halogen, NO_2 , $C(O)R_{10}$, OR_{11} , CH_2OR_{11} , $CH_2NR_{12}R_{13}$, SR_{11} , $NR_{12}R_{13}$, $CONR_{12}R_{13}$, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen;

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or Serial No.: 10/579,263 Examiner: Binta M. Robinson

Date of Office Action: 19 JAN 2010 Applicant(s): Widmer et al. Date of Response: April 19, 2010

R₁₂ and R₁₃, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C₁₋₄ alkyl, hydroxyl, halogen amino, and C(O)OR₁₁:

and when A is $-CH_2-C(O)PhCH_2-Ph-C(O)-CH_2-$, and R_1 and R_4 are hydroxy substituted ethyl, then one of R_2 , R_3 and R_4 is different:

and salts thereof:

or:

(2) Y_1 and Y_2 may be the same or different and are independently selected from N and P;

 R_1 to R_6 may be the same or different and are independently selected from the group consisting of optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, halogen, $O(C_{1-6}$ alkyl), $O(O)O(C_{1-6}$ alkyl), $OC(O)(C_{1-6}$ alkyl), $OC(O)(C_{1$

 R_1 and R_2 together with the Y_1 group to which they are attached, or R_1 , R_2 and R_3 together with the Y_1 group to which they are attached may optionally form a heterocycloalkyl group; and R_4 and R_5 together with the Y_2 group to which they are attached, or R_4 , R_5 and R_6 together with the Y_2 group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from $C_{1.6}$ alkyl, $C_{2.6}$ alkenyl, $C_{2.6}$ alkynyl, hydroxyl, halogen, $O(C_{1.6}$ alkyl), $C(O)O(C_{1.6}$ alkyl), $OC(O)(C_{1.6}$ alkyl), OC_2 amino, hydroxy $C_{1.6}$ alkyl, aryl, OC(O)Ph, and $=C(Ph)_2$;

 R_7 , R_8 and R_8 may be the same or different and are independently selected from F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted $C_{5.7}$ cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from $C_{1.6}$ alkyl, $C_{2.6}$ alkenyl, $C_{2.6}$

Examiner: Binta M. Robinson Date of Office Action: 19 JAN 2010

Applicant(s): Widmer et al.

Date of Response: April 19, 2010

alkynyl, hydroxyl, halogen, NO₂, C(O)R₁₀, OR₁₁, CH₂OR₁₁, CH₂NR₁₂R₁₃, SR₁₁, NR₁₂R₁₃, CONR₁₂R₁₃, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substitutents are independently selected from C_{1-4} alkyl, hydroxyl and halogen:

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or

 R_{12} and R_{13} , together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C_{14} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$;

and salts thereof,

or:

(3) Y₁ and Y₂ are both nitrogen;

 R_1 to R_6 may be the same or different and are independently selected from the group consisting of substituted C_{1-10} alkyl, substituted C_{2-10} alkenyl, substituted C_{2-10} alkynyl, substituted C_{3-10} cycloalkyl, substituted aryl, substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C_{4-6} alkyl, C_{4-6} alkenyl, C_{4-6} alkyl, hydroxyl, C_{1-6} alkyl), C_{4-6} alkyl), C_{4-6} alkyl), C_{4-6} alkyl), C_{4-6} alkyl), C_{4-6} alkyl, aryl, C_{4-6} alkyl, C_{4-6} a

 R_7 , R_7 , R_8 and R_8 may be the same or different and are independently selected from hydrogen, F and Cl:

 R_1 and R_2 together with the Y_1 group to which they are attached, or R_1 , R_2 and R_3 together with the Y_1 group to which they are attached may optionally form a heterocycloalkyl group; and

R₄ and R₅ together with the Y₂ group to which they are attached, or R₄, R₅ and R₆ together with the Y₂ group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, hydroxyl, halogen, O(C₁₋₆ alkyl), C(O)O(C₁₋₆ alkyl), OC(O)(C₁₋₆ alkyl), NO₂, amino, hydroxy C₁₋₆ alkyl, aryl, OC(O)Ph, and =C(Ph)₂;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted C₅₋₇ cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, hydroxyl, halogen, NO₂, C(O)R₁₀, OR₁₁, CH₂OR₁₁, CH₂NR₁₂R₁₃, SR₁₁, NR₁₂R₁₃, CONR₁₂R₁₃, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{2-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen;

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or

 R_{12} and R_{13} , together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from $C_{1:4}$ alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$;

wherein when $-C(R_7R_{7'})$ -(A)- $(CR_8R_{8'})$ - is 9, 10, 11 or 12 alkylene groups and when R_1 , R_2 and Y_1 form a heterocycloalkyl group and when R_4 , R_5 and Y_2 form a heterocycloalkyl group, then R_3 and R_6 are different; and

wherein when $-C(R_1R_7)-(A)-(CR_8R_8)-is 9$, 10 or 12 alkylene groups and R_1 , R_2 , R_3 and Y_1 form a bicyclic group, then R_1 , R_2 , R_3 and Y_1 together are different to R_4 , R_5 , R_6 and Y_2 when taken together,

and salts thereof.

or:

(4) Y₁ and Y₂ are both nitrogen;

 R_1 to R_6 may be the same or different and are independently selected from the group consisting of optionally substituted $C_{1:10}$ alkyl, optionally substituted $C_{2:10}$ alkenyl, optionally substituted $C_{2:10}$ alkenyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substitutents are independently selected from $C_{1:6}$ alkyl, $C_{2:6}$ alkenyl, $C_{2:6}$ alkenyl, $C_{2:6}$ alkynyl, halogen, $O(C_{1:6}$ alkyl), $C(O)O(C_{1:6}$ alkyl), $OC(O)(C_{1:6}$ alkyl), $OC(O)(C_{1:6}$ alkyl), aryl, OC(O)Ph, and OC(O)Ph, and OC(O)Ph, and OC(O)Ph, and OC(O)Ph, aryl, OC(O)Ph, and OC(O)Ph, and OC(O)Ph, and OC(O)Ph, aryl, OC(O)Ph, and OC(O)Ph, and OC(O)Ph, are

 R_1 and R_2 together with the Y_1 group to which they are attached, or R_1 , R_2 and R_3 together with the Y_1 group to which they are attached may optionally form a heterocycloalkyl group; and R_4 and R_5 together with the Y_2 group to which they are attached, or R_4 , R_5 and R_6 together with the Y_2 group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from $C_{1\cdot6}$ alkyl, $C_{2\cdot6}$ alkenyl, $C_{2\cdot6}$ alkynyl, hydroxyl, halogen, $O(C_{1\cdot6}$ alkyl), $C(O)O(C_{1\cdot6}$ alkyl), $O(O)(C_{1\cdot6}$ alkyl), $O(O)(O)(C_{1\cdot6}$ alkyl), $O(O)(O)(C_{1\cdot6}$

 R_7 , R_7 , R_8 and R_8 may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted C_{5-7} cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, halogen, NO_2 , $C(O)R_{10}$, OR_{11} , CH_2OR_{11} , $CH_2NR_{12}R_{13}$, SR_{11} , $NR_{12}R_{13}$, $CONR_{12}R_{13}$, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{2-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen;

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or

R₁₂ and R₁₃, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C_{1.4} alkyl, hydroxyl, halogen, amino, and C(O)OR_{1.1};

wherein when $-C(R_7R_7)$ -(A)- (CR_8R_8) - is 12 alkylene groups, one of R_1 to R_6 is different; and

wherein when $-C(R_7R_7)-(A)-(CR_8R_8)$ is 10 alkylene groups and four of R_1 to R_6 are $C_{1:3}$ alkyl, the remaining two of R_1 to R_6 are different; and

wherein when $-C(R_7R_7)-(A)-(CR_8R_8)-is 9$, 10, 11 or 12 alkylene groups and when R_1 , R_2 and Y_1 form a heterocycloalkyl group and when R_4 , R_5 and Y_2 form a heterocycloalkyl group, then R_3 and R_6 are different; and

wherein when $-C(R_7R_7)-(A)-(CR_8R_8)$ is 9, 10 or 12 alkylene groups and R_1 , R_2 , R_3 and Y_1 form a bicyclic group, then R_1 , R_2 , R_3 and Y_1 together are different to R_4 , R_5 , R_6 and Y_2 when taken together;

and salts thereof

or:

(5) Y₁ and Y₂ are both nitrogen;

 R_1 to R_6 may be the same or different and are independently selected from the group consisting of optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted Serial No.: 10/579,263 Examiner: Binta M. Robinson

Date of Office Action: 19 JAN 2010 Applicant(s): Widmer *et al.* Date of Response: April 19, 2010

 R_1 and R_2 together with the Y_1 group to which they are attached, or R_1 , R_2 and R_3 together with the Y_1 group to which they are attached may optionally form a heterocycloalkyl group; and R_4 and R_5 together with the Y_2 group to which they are attached, or R_4 , R_5 and R_6 together with the Y_2 group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups is substituted with one or more groups selected from C_{4-6} alkyl, C_{4-6} alkynl, hydroxyl, halogen, $O(C_{1-6}$ alkyl), $C(O)O(C_{1-6}$ alkyl), $OC(O)(C_{1-6}$ alkyl), $OC(O)(C_{1-6}$

 R_7 , R_7 , R_8 and $R_{8'}$ may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted C₅₋₇ cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, hydroxyl, halogen, NO₂, C(O)R₁₀, OR₁₁, CH₂OR₁₁, CH₂NR₁₂R₁₃, SR₁₁, NR₁₂R₁₃, CONR₁₂R₁₃, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C_{1.6} alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen;

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or

Examiner: Binta M. Robinson
Date of Office Action: 19 JAN 2010
Applicant(s): Widmer et al.
Date of Response: April 19, 2010

 R_{12} and R_{13} , together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from $C_{1\times 4}$ alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$:

and salts thereof,

wherein when $-C(R_7R_7)$ -(A)- (CR_8R_8) - is 12 alkylene groups, one of R_1 to R_6 is different; and

wherein when $-C(R_7R_7)-(A)-(CR_8R_8)$ is 10 alkylene groups and four of R_1 to R_6 are $C_{1.3}$ alkyl, the remaining two of R_1 to R_6 are different; and

wherein when $-C(R_7R_7)-(A)-(CR_8R_8)-is 9$, 10 or 12 alkylene groups and R_1 , R_2 , R_3 and Y_1 form a bicyclic group, then R_1 , R_2 , R_3 and Y_1 together are different to R_4 , R_5 , R_6 and Y_2 when taken together;

or:

Y₁ and Y₂ are both P;

 R_1 to R_6 may be the same or different and are independently selected from the group consisting of optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, halogen, $O(C_{1-6}$ alkyl), $C(O)O(C_{1-6}$ alkyl), $OC(O)(C_{1-6}$ alkyl), $OC(O)(C_{1$

 R_1 and R_2 together with the Y_1 group to which they are attached, or R_1 , R_2 and R_3 together with the Y_1 group to which they are attached may optionally form a heterocycloalkyl group; and R_4 and R_5 together with the Y_2 group to which they are attached, or R_4 , R_5 and R_6 together with the Y_2 group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from $C_{1.6}$ alkyl, $C_{2.6}$ alkenyl, $C_{2.6}$ alkynyl, hydroxyl, halogen, $O(C_{1.6}$ alkyl), $C(O)O(C_{1.6}$ alkyl), $C(O)O(C_{1.6}$

Examiner: Binta M. Robinson
Date of Office Action: 19 JAN 2010
Applicant(s): Widmer et al.
Date of Response: April 19, 2010

 R_7 , R_7 , R_8 and R_8 may be the same or different and are independently selected from hydrogen. F and Cl:

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted phenyl, optionally substituted C_{5-7} cycloalkyl, and -C(O)-, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, halogen, NO_2 , $C(O)R_{10}$, OR_{11} , CH_2OR_{11} , $CH_2NR_{12}R_{13}$, SR_{11} , $NR_{12}R_{13}$, $CONR_{12}R_{13}$, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, and optionally substituted aralkyl, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen;

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aralkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from $C_{1.4}$ alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$; or

 R_{12} and R_{13} , together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C_{1-4} alkyl, hydroxyl, halogen, amino, and $C(O)OR_{11}$;

provided that the compound of formula (I) is not selected from the following:

Examiner: Binta M. Robinson Date of Office Action: 19 JAN 2010

Applicant(s): Widmer et al. Date of Response: April 19, 2010

 $R_1 \xrightarrow{\oplus} R_2 \xrightarrow{R_1} R_3$

R1 = R2 = R3 = R4 = R5 = R6 = Ma, EL

R1 = R2 = R4 = R5 = Me, R3 = R6 = EL, Pr R1 = R2 = R4 = R5 = EL, R3 = R6 = Me

R1 = R2 = R4 = R5 = Pr, R3 = R6 = Me R1 = R2 = R4 = R5 = allyl, R3 = R6 = Me Et Br. Et OH Et Et

E E

Me OH Me

 $R_1 \xrightarrow{\Theta}$ $N \xrightarrow{R_4} R_6$ R_6

R1 = R2 = R3 = R4 = R5 = R6 = Me, Et, Pr, Bu, pentyl, allyl

R1 = R2 = R4 = R5 = Me, R3 = R6 = Pr, Bu, Decyl R1 = R4 = Me, R2 = R3 = R5 = R6 = Hexyl, allyl

R1 = R4 =Me, R2 = R5 = Bu, R3 = R6 = octyl

 $\begin{array}{c} R_1 \overset{\oplus}{\longrightarrow} \\ R_2 \overset{\downarrow}{\longrightarrow} \\ \otimes \end{array}$

R1 = R2 = R3 = R4 = R5 = R6 = n-Bu, t-Bu, oct

R₁·⊕ R₂·R₃

R1 = R2 = R3 = R4 = R5 = R6 = Me, Et, allyl R1 = R2 = R4 = R5 = Me, R3 = R6 = Pr, pentyl Me O R = Pr, H, pents

it - 11, 11, parity, mays, busys, me, c

R1 = R2 = R4 = R5 = ellyl, R3 = R6 = Et

R₁ ⊕ N R₂ N R₃ R₄

R1 = R2 = R3 = R4 = R5 = R6 = Me, Pr, pentyl, butyl, allyl, ethyl, hexyl R1 = R2 = R3 = R4 = R5 = R6 = Bu, Et, hexyl, heptyl, pentyl, propyl, decyl, i-Pr, octyl

R1 = R4 = Me, R2 = R3 = R5 = R6 = allyl, ethyl R1 = R2 = R4 = R5 = Et, R3 = R6 = hexyl Me Me Me Et

Me OH Me Me

Me OH Me Me

R1 = R2 = R3 = R4 = R5 = R6 = Me, Et R1 = R2 = R4 = R5 = Me, R3 = R6 = pentyl

Examiner: Binta M. Robinson Date of Office Action: 19 JAN 2010

Applicant(s): Widmer et al.

Applicant(s): Widmer et al.

Date of Response: April 19, 2010

$$R_1$$
 R_2
 R_3
 R_3
 R_1
 R_2
 R_3
 R_4
 R_5
 R_5
 R_4
 R_5
 R_5

R1 = R2 = R4 = R5 = Me, R3 = R6 = Bu, Et, heptyl, nonyl,

R1 = R2 = R4 = R5 = allyl, R3 = R6 = Me, Et R1 = R2 = R4 = R5 = hexyl, R3 = R6 = Me

R1 = R4 = Me, R2 = R5 = Et, R3 = R6 = Pr

$$R_1$$
 \oplus R_2 R_3 R_4 R_5 R_4 R_5 R_6 R_6

R1 = R2 = R3 = R4 = R5 = R6 = Me, Et, Bu R1 = R4 = Me, R2 = R5 = Et, R3 = R6 = Pr

$$\begin{array}{c} R_1 \\ R_2 \\ R_3 \\ R_1 = R2 = R3 = R4 = R5 = M6, EL, Pr, eMpt \\ R_1 = R2 = R4 = R5 = M6, R3 = R6 = EL \\ R_1 = R2 = R4 = R5 = EL, R3 = R6 = M6 \end{array}$$

R1 = R2 = R4 = R5 = Et, R3 = R6 = Me R1 = R4 = Me, R2 = R5 = Et, R3 = R6 =

R1 = R2 = R3 = R4 = R5 = R6 = Me, Et R1 = R4 = Me, R2 = R5 = Et, R3 = R6 = Pr

R1 = R4 = Me, R2 = R5 = Et, R3 = R6 = Pr

Examiner: Binta M. Robinson

Date of Office Action: 19 JAN 2010

Examiner: Binta M. Robinson Date of Office Action: 19 JAN 2010

Applicant(s): Widmer et al.

Date of Response: April 19, 2010

2. (Previously Presented): A compound according to claim 1, wherein Y1 and Y2 are each N.

Examiner: Binta M. Robinson Date of Office Action: 19 JAN 2010

Applicant(s): Widmer et al. Date of Response: April 19, 2010

 (Previously Presented): A compound according to claim 1, wherein Y₁ and Y₂ are different.

4. (Previously Presented): A compound according to claim 1, wherein R_1 to R_6 are independently selected from the group consisting of optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkylene, optionally substituted aryl, and optionally substituted heterocycloalkyl, or

 R_1 and R_2 together with the Y_1 group to which they are attached, or R_1 , R_2 and R_3 together with the Y_1 group to which they are attached form a heterocycloalkyl group; and R_4 and R_5 together with the Y_2 group to which they are attached, or R_4 , R_5 and R_6 together with the Y_2 group to which they are attached form a heterocycloalkyl group; wherein said optional substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, halogen, $O(C_{1-6}$ alkyl), $C(O)O(C_{1-6}$ alkyl), $OC(O)(C_{1-6}$ alkyl), $OC(O)(C_{1-6}$ alkyl), $OC(O)(C_{1-6}$ alkyl), and aryl.

- 5. (Previously Presented): A compound according to claim 1, wherein A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted phenyl, and -C(O)-, wherein the substituents are independently selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, hydroxyl, halogen, NO₂, C(O)R₁₀, OR₁₁, CH₂OR₁₁, CH₂NR₁₂R₁₃, SR₁₁, NR₁₂R₁₃, CONR₁₂R₁₃, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl.
- (Previously Presented): A compound according to claim 1, wherein the length of A
 is from 5 to 9 carbon atoms.

Examiner: Binta M. Robinson Date of Office Action: 19 JAN 2010 Applicant(s): Widmer et al. Date of Response: April 19, 2010

7. (Currently Amended): A compound according to claim 1, of Formula (Ia) wherein the bis-cation of the compound is of Formula (Ia):

$$R_1 \oplus R_2 \longrightarrow R_4$$
 $R_2 \longrightarrow R_3 \longrightarrow R_6$
(Ia)

wherein

Y₁ and Y₂ may be the same or different and are independently selected from N and P;

 R_1 and R_2 together with the Y_1 group to which they are attached may optionally form a heterocycloalkyl group; and R_4 and R_5 together with the Y_2 group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from $C_{1.6}$ alkyl, $C_{2.6}$ alkeyl, hydroxyl, halogen, $O(C_{1.6}$ alkyl), $C(O)O(C_{1.6}$ alkyl), amino, hydroxy $C_{1.6}$ alkyl, and aryl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, and optionally substituted phenyl, wherein the length of A is from 5 to 18 carbon atoms, and wherein the substituents are independently selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, halogen, C(O)R₁₀, OR₁₁, SR₁₁, CH₂OR₁₁, CH₂NR₁₂R₁₃, NR₁₂R₁₃, CONR₁₂R₁₃, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{3-10} cycloalkyl, wherein said optional substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, and hydroxyl;

Serial No.: 10/579.263 Examiner: Binta M. Robinson

Date of Office Action: 19 JAN 2010 Applicant(s): Widmer et al.

Date of Response: April 19, 2010

R₁₂ and R₁₃ are independently selected from the group consisting of hydrogen, optionally substituted C₁₋₁₀ alkyl, optionally substituted C₂₋₁₀ alkenyl, optionally substituted C₂₋₁₀ alkynyl, optionally substituted C3-10 cycloalkyl, optionally substituted alkylheteroaryl, wherein said substituents are independently selected from C_{1.6} alkyl, C_{2.6} alkenyl, aryl, hydroxyl, halogen, amino, and C(O)OR11; or

R₁₂ and R₁₃, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, hydroxyl, halogen, amino, and C(O)OR₁₁₇ and salts thereof.

8. (Previously Presented): A compound according to claim 1, selected from 1,11-bis-(tributylammonium)undecane, 1,16-bis-(tributylammonium)hexadecane, 1,12-bis-(tripentylammonium)dodecane, 1,12-bis-(trihexylammonium)dodecane, 1,12-bis-(trioctylammonium)dodecane, 1,12-bis-(triisobutylammonium)dodecane, 1,12-bis-(triisopentylammonium)dodecane, and 1.12-bis-(1-butylpyrrolidinium)dodecane, and salts thereof

9. (Withdrawn): A method for one or more of treating, inhibiting, and preventing a bacterial or fungal infection in a vertebrate, said method comprising administering to said vertebrate an effective amount of at least one compound of Formula (II):

$$\begin{array}{c}
R_1 \oplus \\
R_2 \longrightarrow Y_1 - C(R_7R_7) - (A) - C(R_8R_8) - Y_2 \longrightarrow R_5 \\
R_8 \longrightarrow R_8
\end{array}$$
(II)

wherein

Y₁ and Y₂ may be the same or different and are independently selected from N and P;

 R_1 to R_6 may be the same or different and are independently selected from the group consisting of optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heterocycloalkyl, wherein said substituents are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, halogen, $O(C_{1-6}$ alkyl), $O(O)O(C_{1-6}$ alkyl), $O(O)P_1$, and $O(O)P_2$, armino, hydroxyl, and $O(O)P_3$, aryl, $O(O)P_4$, and $O(O)P_5$, and $O(O)P_5$, and $O(O)P_6$, and and an analysis a

 R_1 and R_2 together with the Y_1 group to which they are attached, or R_1 , R_2 and R_3 together with the Y_1 group to which they are attached may optionally form an heterocycloalkyl group; and R_4 and R_5 together with the Y_2 group to which they are attached, or R_4 , R_5 and R_6 together with the Y_2 group to which they are attached may optionally form a heterocycloalkyl group; wherein each of said heterocycloalkyl groups may be optionally substituted with one or more groups selected from $C_{1.6}$ alkyl, $C_{2.6}$ alkynyl, $C_{2.6}$ alkynyl, hydroxyl, and halogen, $O(C_{1.6}$ alkyl), $O(O(C_{1.6}$ alkyl), $O(C_{1.6}$ alkyl), $O(C_{1.6})$ alkyl), $O(C_{1.6})$

 R_7 , R_7 , R_8 and R_8 may be the same or different and are independently selected from hydrogen, F and Cl;

A comprises one or more groups selected from optionally substituted alkylene, optionally substituted alkenylene, optionally substituted phenyl, optionally substituted C₅₋₇ cycloalkyl, and -C(O)-, wherein the length of A is from 4 to 18 carbon atoms, wherein the substituents are independently selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, hydroxyl, halogen, nitro, C(O)R₁₀, OR₁₁,

CH₂OR₁₁, CH₂NR₁₂R₁₃, SR₁₁, NR₁₂R₁₃, CONR₁₂R₁₃, amino acids, dipeptidyl, tripeptidyl, tetrapeptidyl and pentapeptidyl;

R₁₀ is selected from OH, OR₁₁, C₁₋₆ alkyl, optionally substituted amino-C₁₋₆-alkylsulfonate, optionally substituted amino-C₁₋₆-alkylphophonate, optionally substituted amino-C₁₋₆-alkyl-guanidinyl, and optionally substituted amino-C₁₋₆-alkyl-tri(C₁₋₆-alkyl)ammonium;

 R_{11} is selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{2-10} alkyl, optionally substituted aryl, optionally substituted arylakyl, optionally substituted amino- C_{1-6} -alkylsulfonate, optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} -alkyl-tri(C_{1-6} -alkyl)-ammonium, wherein said optional substituents are independently selected from C_{1-4} alkyl, hydroxyl and halogen

 R_{12} and R_{13} are independently selected from the group consisting of hydrogen, optionally substituted C_{1-10} alkyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{2-10} alkynyl, optionally substituted alkylheteroaryl, optionally substituted amino- C_{1-6} - alkylsulfonate, optionally substituted amino- C_{1-6} -alkylphophonate, optionally substituted amino- C_{1-6} -alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-guanidinyl, and optionally substituted amino- C_{1-6} -alkyl-tri(C_{1-6} - alkyl-tri(C_{1-6} - alkyl

R₁₂ and R₁₃, together with the nitrogen atom to which they are attached may form an optionally substituted heterocycloalkyl group, wherein said substituents are independently selected from C₁₋₃ alkyl, hydroxyl, halogen, amino, and C(O)OR₁₁.

- 10. (Withdrawn): The method according to claim 9, wherein said compound is a compound of Formula (I) as defined in claim 1.
- 11. (Withdrawn): The method according to claim 9, wherein the infection is a fungal infection.

Examiner: Binta M. Robinson

Date of Office Action: 19 JAN 2010 Applicant(s): Widmer et al.

12. (Withdrawn):

Date of Response: April 19, 2010

The method according to claim 9, wherein the infection is a

bacterial infection.

13. (Withdrawn): A method of inhibiting phospholipase in an organism comprising contacting said organism with an effective amount of at least one compound of Formula (I) or at least one compound of Formula (II).

14. (Withdrawn): The method according to claim 13, wherein the organism is selected from bacteria, fungi, virus, and parasite.

15. (Withdrawn): The method according to claim 13, wherein the phospholipase is Phospholipase B.

16. (Withdrawn): The method according to claim 13, wherein the organism is selected from the group consisting of: bacteria, fungi and virus.

17. (Withdrawn): A method for identifying an antimicrobial agent comprising contacting microbial cells with a compound of Formula (I) or Formula (II) suspected of having antimicrobial properties, determining whether said compound inhibits a microbial phospholipase enzyme, wherein inhibition of said phospholipase enzyme indicates antimicrobial activity, and thereby identifying an antimicrobial agent.

18. (Canceled).

19. (Canceled).